

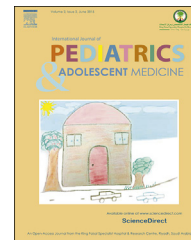
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## ORIGINAL RESEARCH ARTICLE

# BCG related complications: A single center, prospective observational study



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Received 12 March 2015; received in revised form 18 May 2015; accepted 22 May 2015

Available online 11 June 2015

## KEYWORDS

Bacillus Calmette  
–Guerin;  
Lymphadenitis;  
Tuberculosis

**Abstract** *Background and objectives:* Although the BCG vaccine is usually a safe vaccine, a number of complications can occur, such as adverse local reactions, regional lymphadenitis, osteomyelitis and disseminated infection in immunocompromised children, with lymphadenitis being the most common complication. Our objective to describe the associated clinical characteristics and outcomes.

*Materials and methods:* This was a prospective observational study conducted over two year's period.

*Results:* 100 patients were enrolled with (62%) males and (38%) females. 93 cases (93%) have nodes involvement with a total of 103 nodes was reported as follow: Axillary, supraclavicle, cervical with number of 75(72.8%), 23(22.3%), 5(4.9%) respectively. (55.3%) resulted in suppuration, and (44.7%) with non-suppuration. Only 3 cases (3%) had severe disease with dissemination, (88.3%) had small size nodes (< 3 cm), and (11.7%) with large size nodes (>3 cm). (88%) had self-limited disease, and node disappears between (8–168 weeks).

*Conclusion:* In the Majority of BCG related lymphadenitis is a benign condition with spontaneous healing. Also there is Increase incidence of association between BCG vaccine and serious disseminated infections in immunodeficiency cases.

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## 1. Introduction

Bacillus Calmette–Guerin (BCG) is a live attenuated vaccine derived from a strain of *Mycobacterium bovis* with a characteristics residual virulence, has been used to prevent tuberculosis since 1921 [1].

The World Health Organization (WHO) has recommended BCG vaccination as part of the global Expanded Program for

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Peer review under responsibility of King Faisal Specialist Hospital & Research Centre (General Organization), Saudi Arabia.

Immunization (EPI). Since Saudi Arabia has an annual tuberculosis (TB) incidence rate of 15 cases/100,000 people, the national immunization Program still includes neonatal BCG vaccination [2]. As of to date the BCG vaccine strain which is use to vaccinate babies in Saudi Arabia is Dannish Strain. Although the BCG vaccine is usually a safe vaccine, a number of complications can occur, such as adverse local reactions, regional lymphadenitis, osteomyelitis and disseminated infection in immunocompromised children, with lymphadenitis being the most common complications [3].

We conducted this study to describe children with BCG vaccine related complications and highlight their presentation, course and treatment options.

## 2. Materials and methods

This study was conducted at King Fahad Medical City –Children’s Specialized Hospital, Riyadh. The hospital provides all levels of care for Riyadh City region as well as a referral center from all over the Kingdom of Saudi Arabia. All children who were referred to pediatric infectious disease clinics with any BCG vaccine complications were enrolled, date included between June 2011 and June 2013. All children had received the same type of vaccine (Danish strain) at birth administered intradermally at the governmental Centers. We used a standardized case report form with different variables. And all patients were followed prospectively till one year from their initial presentation with documented progress.

Data were presented as numbers (percentages), and median [minimum – maximum].

## 3. Results

A total of 100 children referred to infectious diseases Clinics as case of BCG vaccine related complications. Of whom 62 children (62%) were males and 38 (38%) were females (Table 1). (92%) were immunocompetent while only 8% were immunocompromised: 4 (4%) IL12 deficiency, 2 (2%) CGD, 1 (1%) SCID, 1 (1%) HIV, respectively.

**Table 1** Children characteristics (No: 100 children).

<b>Gender: number (%)</b>	
Male	62 (62)
Female	38 (38)
Median age at starting symptoms (weeks)	8 [3–46]
Median age at presentation (weeks)	16 [6–48]
<b>Type of complication: number (%)</b>	
Regional lymphadenitis	90 (90)
Disseminated (BCG iosis)	3 (3)
Local reaction (ulcer, discharge, abscess)	7 (7)
<b>Immune status: number (%)</b>	
Immunocompetent	92 (92)
Immunocompromised	8 (8)
Data are presented as number (%) and median [minimum–maximum].	

Age at observed symptoms ranged between 3 and 46 weeks with a median of 8 weeks. While the time of initial presentation to the hospital was (6–48) weeks with a median of 16 weeks. 93 children (93%) have nodes involvement with a total of 103 nodes was reported as follow: Axillary, supraclavicle, cervical with number of 75 (72.8%), 23 (22.3%), 5 (4.9%) respectively. 91 (88.3%) of the nodes had small size (< 3 cm) while 12 nodes (11.8%) with large size (>3 cm).

57 cases (55.3%) resulted in suppuration, of which 50 cases (87.7%) the abscess ruptured, of which 2 (4%) complicated by superimposed bacterial infection. 46 cases (44.7%) were non suppurative lymphadenitis (Table 2). Node disappears between (8–168 weeks) with a median of 32 weeks. Delayed nodes healing was mostly observed in immunocompromised children.

Out of the 100 children; 16 (16%) have local reaction at BCG site in form of discharge scars or subcutaneous abscess or ulceration, Nine of them with associated lymph node and seven with only local complications. and 3 (3%) had severe disease with dissemination (BCGiosis) (Table 1), and all were immunocompromised with Interleukin-12 (IL 12) deficiency disease.

The treatment given for these children was assisted as follow: 84 children (84%) had no treatment due to self-limited disease, while 16 (16%) end with treatment as follow: 11 (9%) with antituberculus treatment, 2 (2%) with surgical intervention, and 3 (3%) with both medical and surgical intervention.

## 4. Discussion

In this study, we explored a common but relatively under recognized problem of post BCG lymphadenopathy.

Post BCG vaccination complications are well recognized [4]. Mild adverse reactions are considered as part of the normal reaction [4]. The reported incidence of these events worldwide is 0.1–17% [5].

The explanation is not fully clear for the noted increase in BCG related complications [6,7]. The frequency of the lymphadenitis after vaccination correlates with the type of vaccine used. Teo et al [8] had demonstrated an increase in the incidence of lymphadenitis after the introduction of Danish strain (SSI) type in the United Kingdom. Using this

**Table 2** Node characteristics (No: 103 nodes).

<b>Node involved: number (%)</b>	
Axillary	75 (72.8)
Supraclavicle	23 (22.3)
Cervicle	5 (4.9)
<b>Type of the node complication: number (%)</b>	
Suppurative	57 (55.3)
Ruptured	50 (87.7)
Non ruptured	7 (12.3)
Non suppurative	46 (44.7)
Disseminated (BCG iosis)	3 (3)
Local reaction (ulcer, discharge, abscess)	16 (16)
<b>Size of the node: number (%)</b>	
<3 cm	91 (88.3)
>3 cm	12 (11.7)

type of vaccine, there is a potential error in dosing, Infants less than 1 year should receive a 0.05 ml in contrast to 0.1 ml dose in using the older types [7,8]. The use of a more reactogenic strain of this vaccine may also explain such complications. Characteristics of the recipient population may also be a determinant factor in the risk for complications [7,8]. This may account for the difference in incidence of complications in different countries. Mori et al [5] confirmed the age related reported complications; highest risk of lymphadenopathy is reported in newborn period [7–9].

Unilateral axillary lymph node enlargement was seen in 75 infants (75%), this is consistent with what is most commonly seen in a previous study [9,10].

The majority of BCG lymphadenitis develops around 8 weeks after BCG vaccination. The time of node swelling correlates with the peak of local cutaneous reaction to the vaccine [5–9].

In our study, suppurative lymphadenitis was seen in 57 nodes (55.3%) which is consistent with what have been found in other study (30–80%) [11].

Disseminated BCG infection is rare complication with estimated incidence of 0.1–4.3 per one million vaccinated children but is lethal in 50–71% of the cases [12,13]. The death rate is especially higher in cases of immunodepression (83%) and it is important to note that a temporary or permanent immune deficiency is observed in 86% of the cases [6–12]. However, in some area, the rate of Disseminated BCG infection even higher which is reaching 22.9% and the mortality rate is 72.8% [14]. One of the major immunodeficiency diseases leading to dissemination of BCG is defect of 1L–12/INF – gamma axis and can often be lethal [15]. In our study dissemination disease (BCGiosis) rate was 3% and all cases with 1L-12/INF – gamma axis defect as a cause of immunodeficiency.

Otherwise, BCG regional lymphadenitis is a self-limiting complication with no need for either medical or surgical intervention. Is in contrast to the previous practice in the Kingdom where antituberculous medications were used commonly [15]. Nevertheless, we noticed occasionally that we could avoid node excision in case of large node size by using isoniazid with or without Rifampin for a period. However, this may relate to the susceptibility of our current strain (Dannish), in difference to which other studies reported that introduction of antituberculous medications did not show change in outcome of the large size node (>3 cm) [16].

Our findings are not in accordance with a previous Saudi study [15] which was showed that medical treatment in addition to needle aspiration were the most effective treatment for enlarged lymph nodes. Abdullah et al [17] reported five cases among eight patients with iatrogenic sinus formation following needle aspiration. In contrast to, Paul Hengster et al [18] who proved the success of surgical excision for the lymph node when it is exceeding 1.5 cm especially in reducing the healing time. Also in contrast to other studies [19,20] that demonstrated a sinus formation following the self-rupture as a burden we rarely referred a patient for surgical treatments (Needle aspiration/Excision) even with large size suppurative node that got healed with no complications following puncture.

## 5. Conclusion

Majority of BCG related lymphadenitis is a benign condition, and have spontaneous healing. Occasionally, with large size node, introducing of an antituberculous medications and/or surgical intervention will be as useful. This prospective study also shed light on a high rate of association between BCG vaccine and serious disseminated infections especially in immunodeficiency cases. Thus, it would be advisable to administer BCG vaccine at a time later than at birth.

## Conflict of interest

Authors have no conflicts of interest to disclose.

## Acknowledgments

We thank Dr Mohammed ALTannir for reviewing the study, as well as Ms. Mona AlHarthi for her assistance in collecting the data.

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